REMARKS

Claims 3-7, 9-13 and 16-19 presently appear in this case. No claims have been allowed. The official action of December 5, 2000, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a method of ameliorating the degenerative effects of injury or disease on the central nervous system or peripheral nervous system by preventing or inhibiting axonal degeneration and/or promoting nerve regeneration. It has been discovered that NS-specific anti-self-activated T cells accumulate at a site of injury or disease of the CNS or PNS and have a neuroprotective effect. Thus, the method comprises the administration of such T cells, or antigens or peptides which activate T cells *in vivo* to produce such a population of T cells, or a nucleotide sequence which encodes such a NS-specific antigen or peptide for the purpose of activating such T cells.

With respect to the election/restriction requirement, the examiner states that it does not matter that both groups I and II are recited in a single claim as the inventions are separable in that they achieve different effects as claimed, may be differently classified, and require different searches. The examiner states that the requirement is still deemed proper and, therefore, made final. The

examiner states that there being no allowable generic or linking claim, claim 16 is only being examined to the extent of the elected species. The examiner has required that applicants set forth the claims in accordance with the elected invention. The restriction requirement is again respectfully traversed.

It is respectfully submitted that the examiner is incorrect in stating that the two groups, as claimed in claim 16, are separable in that they achieve different effects as claimed. Claim 16 is directed to a method of ameliorating the degenerative effects of injury or disease on the central nervous system or peripheral nervous system. This is achieved by preventing or inhibiting axonal degeneration and/or promoting nerve regeneration. Thus, the effect of group I (a method of preventing or inhibiting axonal degeneration) and group II (a method of promoting nerve regeneration) are the same as claimed, i.e., ameliorating the degenerative effects of injury or disease on the CNS or PNS. As claim 16 is a valid generic claim, both groups and all species must be examined once the generic claim is found to be allowable.

The examiner's requirement to "set forth the claims in accordance with the elected invention" is respectfully traversed. There is no justification in the rules or MPEP practice for requiring an applicant to "set forth the claims

in accordance with the elected invention", particularly at this early stage of prosecution. First of all, 37 C.F.R. §1.144 states that any petition from a restriction requirement can be deferred until after final action or on allowance of claims to the invention elected. Furthermore, the generic claims must be examined once the elected species is found to be allowable. An applicant cannot be required to delete generic claims before examination of the elected species is completed. Accordingly, reconsideration and withdrawal of the restriction requirement is again respectfully urged.

Claims 3-5 have been objected to under 37 C.F.R. §1.75(c) as being of improper dependent form. The examiner states that claims 3-5 recite the method of claim 16, wherein the method is for ameliorating the effects of different diseases and injuries, but the recitation of different diseases and injuries fails to further limit the method or effects as claimed and, thus, do not further limit the parent claim. The examiner states that the injuries and diseases do not further distinguish the method and, thus, such limitations are not deemed to receive patentable weight. This objection is respectfully traversed.

Even if the examiner chooses to disregard the statements in the preamble as being limitations, the first step of the method is, "administering to a human in need

thereof an effective amount ...". Thus, the human to which the composition is administered will differ depending on the disease or injury being treated. In order to clarify this, claims 3-5 have now been amended to specify that "said human" is one having said injury or disease. MPEP §608.01(n)(III) states that the test as to whether a claim is a proper dependent claim is the infringement test. Thus, if independent claim 16 can be infringed by any method which would not infringe dependent claim 3, for example, then dependent claim 3 further limits claim 16. Administering MBP to a patient with Alzheimer's Disease will infringe claim 16 but will not infringe claim 3, as claim 3 requires that the patient being treated is one having an injury selected from the group set forth in that claim. Thus, the dependent claims further limit the independent claim and are proper dependent claims. Reconsideration and withdrawal of this objection are respectfully urged.

Claims 16, 3-7, 13 and 19 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The examiner states that, while the claims are drawn broadly to ameliorating effects of injury or disease, effects other than retinal ganglion cell survival fail to meet the written description provision of 35 U.S.C. §112, first paragraph. The examiner states that the

applicable law provides that applicant must convey with reasonable clarity that he or she was in possession of the invention and that the invention, for the purposes of the "written description" inquiry, is whatever is now claimed. The examiner states that, with the exception of retinal ganglion cell survival, the skilled artisan cannot envision the effects encompassed by the claims with respect to the recited injuries and diseases and, thus, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. The examiner states that written description requires more than a mere statement of what is part of the invention and that, as only retinal ganglion cell survival but not the full breadth of claims meet the written description provision, the claims are rejected. This rejection is respectfully traversed.

First of all, claim 16 has now been amended to specify that the effects being ameliorated are "degenerative effects". As will be discussed below, this is supported by the specification, for example, at page 4, lines 21-23. The examiner is correct that the applicable law specifies that the written description requirement is fully satisfied if applicant conveys with reasonable clarity that he or she was in possession at the time the application was filed of

whatever is now claimed. What is now claimed is "a method of ameliorating the degenerative effects of injury or disease on the central nervous system or peripheral nervous system, by preventing or inhibiting axonal degeneration and/or promoting nerve regeneration." Clearly, those of ordinary skill in the art would be aware that applicants were in possession of this invention at the time the application was filed in view of the disclosure, for example, on page 4, lines 13-31, and page 23, line 18, to page 24, line 13. Certainly, the skilled artisan can envision that the degenerative effects of injury or disease on the CNS or PNS can be ameliorated if the administration of the present invention causes the prevention or inhibition of axonal degeneration and/or promotion of nerve regeneration. Any more specific effects need not be in the specification as long as they are not in the claim.

The doctrine of simultaneous conception and reduction to practice is only applicable to unusual situations and is the exception to the rule. The examiner has not established why the present application should be considered to be such an exception. If axonal degeneration is prevented or inhibited and/or nerve regeneration is promoted by the administration of the present invention, then those of ordinary skill in the art would readily understand that the degenerative effects of injuries or diseases of the CNS or PNS

will be ameliorated. This is all that is necessary to convey that the applicants were in possession of the invention at the time the application was filed and that the written description requirement of the first paragraph of 35 U.S.C. §112 has been satisfied. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claims 16, 3-7, 13 and 19 have been rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for increased retinal ganglion cell survival following optic nerve crush by administration of NS-specific antigens MOG and MBP, does not reasonably provide enablement for ameliorating the effects of a disease or injury as claimed. The examiner states that the claims encompass all effects of injury and disease, including effects that have nothing to do with nerve regeneration. However, the specification fails to exemplify alleviation of such effects by means of the present invention. Furthermore, the examiner states that neuronal cells exhibit different propensities for degeneration and survival and, thus, the skilled artisan would not expect similar effects of any given treatment in different model systems, particularly to neuronal cells of the peripheral and central nervous systems. Further, the examiner states that the claims are directed to NS-specific antigen derivatives and epitopes, but the artisan recognizes the

unpredictability in the art associated with the prediction of peptide function based on divergent structure. The examiner also states that the specification does not provide guidance as to what amount is required to ameliorate any effects which are not specified in relation to the recited diseases and injuries. Thus, the examiner concludes that the skilled artisan would require further undue experimentation to make and use the invention as claimed. This rejection is respectfully traversed.

First of all, as to the breadth of the term "effects", claim 16 has been amended to specify that the effects are "degenerative effects". As the present specification contends that the administration of the present invention will prevent or inhibit axonal degeneration and/or promote nerve regeneration, it would be expected that this function will cause the amelioration of the degenerative effects of injury or disease on the CNS or PNS. Thus, specifying "degenerative effects" appears to eliminate much of the examiner's initial argument.

As to the requirement for additional model systems in order for the broad assertion of the effects of the present invention to be credible, applicants have experimented with other model systems and shown them also to be operable. Attached hereto are two papers from the laboratory of the

present inventors relating to such experiments: Hauben et al, "Passive or active immunization with myelin basic protein promotes recovery from spinal cord contusion", J Neurosci 20(17):6421-6430 (2000); Hauben et al, "Autoimmune T cells as potential neuroprotective therapy for spinal cord injury", Lancet 355(9200):286-287 (2000). A declaration is presently being prepared confirming the truth and accuracy of the experimentation detailed in these papers. As the statements in the present invention have now been confirmed in two different models, one being the optic nerve crush injury model, and the other being the spinal cord injury model, there is no longer reason to believe that the broad statements of utility in the present specification are incredible.

With respect to the NS-specific antigen derivatives and epitopes and the examiner's statement that one cannot predict peptide function based on divergent structure, it should be understood that the only function which is being claimed for these various peptide structures is the ability to activate T cells. In this regard, reference is made to page 19, lines 16, to page 20, line 13, defining the peptides and derivatives of the present invention. In light of this definition, it would not involve undue experimentation to determine whether the various peptides or derivatives maintain the functional ability to elicit a human T cell response.

With respect to the examiner's comments about "an effective amount", this has been obviated by specifying that the effective amount is an amount effective for neuroprotection. As this term is not indefinite, for the reasons discussed below, there is no reason to believe that undue experimentation would be involved to determine such effective amounts. Note *Ex parte Skuballa*, 12 USPQ2d 1570, 1571 (Bd Pat App & Int'f 1989) which states that a claim to an "effective amount" of a certain compound is not indefinite even though the specification recites "diverse utilities". The Board stated:

> We are satisfied that the skilled worker in this art could readily optimize effective dosages and administration regimens for each of the recited utilities.

Accordingly, reconsideration and withdrawal of this rejection are respectfully urged.

Claims 16, 3-7, 13 and 19 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The examiner states that the term "effective amount" is a relative term in view of the fact that there is no stated function or effect to be achieved. The examiner states that the metes and bounds of "effects" being ameliorated are indefinite because there are no effects specified. This rejection is respectfully traversed.

With respect to "effective amount", claim 16 has now been amended to specify "an effective amount for neuroprotection". This is supported, for example, by the paragraph at page 4, lines 13-31, of the present specification. Similarly, the term "effect" has been amended to read "degenerative effect". This language is also supported by the same paragraph of the specification. As the required function is now set forth in the claim, this part of the rejection has now been obviated.

The examiner states that acknowledgement has been made to applicants' claim for foreign priority, but that a certified copy of the application has not yet been received.

A certified copy of Israel application IL 124550, filed May 19, 1998, will be filed in due course.

Claims 16, 3-7 and 13 have been rejected under 35 U.S.C. §102(b) as being anticipated by Ling. The examiner states that Ling teaches administration of MBP(87-99) to animals suffering from EAE, a model which mimics multiple sclerosis, and that this administration inherently provides an effective amount as required by the present claims. The examiner states that EAE is a form of neuronal degeneration. This rejection is respectfully traversed.

The examiner is incorrect in stating that EAE is a form of neuronal degeneration. EAE, like MS, involves

degeneration of myelin and not degeneration of neurons. Claim 16 is directed to the administration to a human in need of the prevention or inhibition of axonal degeneration and/or promotion of nerve regeneration. EAE subjects or MS patients are in need of myelin regeneration or the prevention of myelin degeneration. Furthermore, it is not understood why the examiner applies this rejection to claims 3 and 4 as these claims comprehend the treatment only of specific injuries and diseases, all of which are quite different from EAE and MS. Additionally, neurological assessment by clinical score is not a measurement of neuronal degeneration. There is no mention of "neuronal degeneration" anywhere in the disclosure of Ling. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claims 16, 3-7, 13 and 19 have been rejected under 35 U.S.C. §102(e) as being anticipated by Weiner. The examiner states that Weiner teaches administration of MBP to ameliorate disease and injury brought about by neuronal degeneration as measured by histological examination clinical score. This rejection is respectfully traversed.

Weiner, like Ling, deals with the treatment of multiple sclerosis. As indicated above, MS involves degeneration of myelin and not degeneration of neurons. Thus, MS is not a disease in which patients are in need of the

prevention or inhibition of axonal degeneration and/or the promotion of nerve regeneration. There is no mention of neuronal degeneration anywhere in Weiner. Accordingly, this rejection must fall for the same reasons as discussed above with respect to Ling. Reconsideration and withdrawal thereof are, therefore, respectfully urged.

It is submitted that all the claims now present in the case clearly define over the references of record. Reconsideration and allowance are, therefore, earnestly solicited.

Respectfully submitted,

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Version with Markings to Show Changes Made

3 (Twice-Amended). A method in accordance with claim 16, wherein said method is for ameliorating the effects of an injury selected from the group consisting of blunt trauma, penetrating trauma, hemorrhagic stroke, ischemic stroke, and damages caused by surgery, and wherein said human is one having said injury.

4 (Twice-Amended). A method in accordance with claim 16, wherein said method is for ameliorating the effects of a disease selected from the group consisting of ~~Diabetic~~ diabetic neuropathy, senile dementia, Alzheimer's disease, Parkinson's Disease, facial nerve (Bell's) palsy, glaucoma, Huntington's chorea, amyotrophic lateral sclerosis, non-arteritic optic neuropathy, and vitamin deficiency, and wherein said human is one having said disease.

5 (Twice-Amended). A method in accordance with claim 16, wherein said method is for ameliorating the effects of a disease which is not an autoimmune disease or a neoplasm, and wherein said human is one having said disease.

16 (Amended). A method of ameliorating the degenerative effects of injury or disease on the central nervous system or peripheral nervous system, by preventing or inhibiting axonal degeneration and/or promoting nerve regeneration, comprising administering to a human in need

thereof an effective amount for neuroprotection of a composition comprising an agent selected from the group consisting of:

(a) non-recombinant, NS-specific antiself activated T-cells;

(b) a NS-specific antigen or a derivative thereof;

(c) a peptide derived from a NS-specific antigen or a derivative thereof;

(d) a nucleotide sequence encoding a NS-specific antigen;

(e) a nucleotide sequence encoding a peptide derived from a NS-specific antigen; and

(f) any combination of (a)-(e).